## Analysis of dose-response trend in mouse for hemangioma -hemangiosarcoma separately

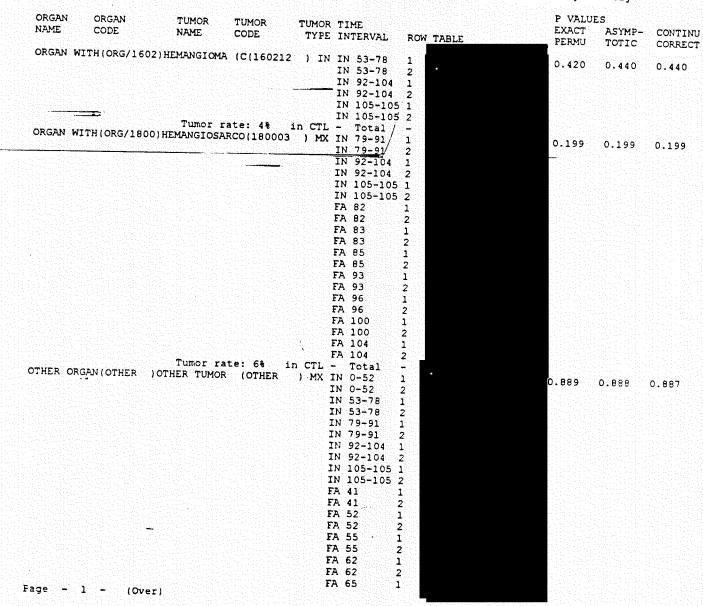
Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend Ted Guo, PH.D, CDER/FDA Run Date & Time: March 19, 1997 (8:34)

Note:

Source: c:\\_data\hemice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively



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Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 19, 1997 (8:34)

Source: c:\\_data\hemice.txt

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Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500) For missing Tumor-Caused-Death set INCIDENTAL

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ORGAN P VALUES ORGAN TUMOR TUMOR TUMOR TIME NAME EXACT CODE NAME ASYMP-CONTINU CODE TYPE INTERVAL ROW TABLE PERMU TOTIC CORRECT FA 65 FA 66 FA 66 FA 70 FA 70 FA 71 FA 71 FA 72 FA 72 FA 74 FA 74 FA 78 FA 78 FA 80 FA 80 FA 81 FA 81 FA 82 FA 82 FA 83 1 2 1 2 FA 83 FA 84 FA 84 FA 85 1 2 1 2 FA 85 FA 88 FA 88 FA 89 1 FA 89 2 FA 90 1 FA 90 2 FA 91 1 FA 91 2 FA 93 1 2 FA 93 FA 94 FA 94 2 FA 96 1 FA 96 FA 98 FA 98 FA 99 1 FA 99 2 1 2 FA 100 FA 100 FA 101 FA 101 2 FA 102 1 FA 102 2 Page - 2 -(Over)

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Analysis of Carcinogenic Potential in Male Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 19, 1997 (8:34)

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ORGAN ORGAN NAME CODE	TUMOR TUMOR NAME CODE	TUMOR TIME	P VALUES EXACT ASYMP- CONTINU
	NAME CODE	TYPE INTERVAL ROW TABLE	PERMU TOTIC CORRECT
		FA 103 1	
		FA 103 2 FA 104 1	
	Tumor 070	FA 104 2	
Page - 3 - (En	nd of File)	in CTL - Total	
Page - 3 - (En	Tumor rate: 87% ad of File)	FA 104 1	

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Analysis of Carcinogenic Potential in Temale Mouse Analysis of Carcinogenic Potential in remaie Mouse
Test of Dose-Response (Tumor) Positive Linear Trend
Ted Guo, PH.D. CDER/FDA
Run Date & Time: March 19, 1997 (8:40)
Source: c:\\_data\hemice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

Note:

For missing Tumor-Caused-Death set INCIDENTAL

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively

NAME	ORGAN	TUMOR TUMOR	TUMOR	TUMOR	TTME			P VALUES		
	CODE	NAME	CODE	TYPE	INTERVAL	ROW	TABLE	EXACT PERMU	ASYMP- TOTIC	CONTINU
ORGAN	WITH (ORG/16	02) HEMANGIOMA	(C(160212	) IN	IN 0-52	1	- Carrier and Carrier and Carrier	0.283		
					IN 0-52	2		0.283	0.278	0.278
					IN 79-91	1				
					IN 79-91	2				
					IN 92-104	1				
					IN 92-104	2				
ΔN	WITH (ODG/10	Tumor ra	te: 2%	in CTL	- Total	-				
	(OKG/18	00) HEMANGIOSAF	KCO(180003	) MX		1		0.481	0.494	0.494
					IN 79-91	2				
					IN 92-104	1				
					IN 92-104	2				
					FA 69	1				
						/2				
					FA 82 /					
					FA 85 /	2				
					FA 85 /	2				
					FA 91	1				
					FA 91	2				
					FA 94	ī				
					FA 94	2				
		Tumor ra	te: 4% i	n CTL	- Total	<u> </u>				
R	ORGA (OTHER	OTHER TUMOR	(OTHER	) MX	IN 0-52	1		0.188	0 100	0.00
					IN 0-52	2		0.188	0.189	0.190
								0.188	0.189	0.190
					IN 0-52	2		0.188	0.189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91	2		0.188	0.189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91	2 1 2 1 2		0.188	0.189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104	2 1 2 1 2			0.189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104	2 1 2 1 2 1 2		0.188	0.189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28	2 1 2 1 2 1 2 1 2		0.188	V-189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 28	2 1 2 1 2 1 2 1 2 1 2		0.188	0.189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 28 FA 30	2 1 2 1 2 1 2 1 2 1 2 1 2		0.188	V-189	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 FA 28 FA 28 FA 30 FA 30	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1			V.169	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 33	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 30 FA 33 FA 33	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 28 FA 30 FA 30 FA 33 FA 33	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1		V.186		0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 FA 28 FA 28 FA 30 FA 30 FA 30 FA 33 FA 33	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1			V-169	0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 30 FA 30 FA 30 FA 30 FA 39 FA 39	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
					IN 0-52 IN 53-78 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 33 FA 33 FA 33 FA 43	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
				, 1 1 1 1 1	IN 0-52 IN 53-78 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 33 FA 33 FA 33 FA 43	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
					IN 0-52 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 30 FA 30 FA 30 FA 30 FA 30 FA 33 FA 39 FA 39 FA 43 FA 43 FA 43 FA 43 FA 43 FA 50 FA 50	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
					IN 0-52 IN 53-78 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 FA 28 FA 28 FA 30 FA 30 FA 33 FA 33 FA 33 FA 33 FA 33 FA 35 FA 37 FA 50 FA 50 FA 50 FA 50	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
					IN 0-52 IN 53-78 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 FA 28 FA 28 FA 30 FA 30 FA 30 FA 33 FA 33 FA 39 FA 39 FA 39 FA 39 FA 43 FA 50 FA 50 FA 52 FA 52	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
				i i i i i i i i i i i i i i i i i i i	IN 0-52 IN 53-78 IN 53-78 IN 53-78 IN 79-91 IN 79-91 IN 92-104 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 33 FA 33 FA 33 FA 33 FA 33 FA 35 FA 37 FA 37 FA 38 F	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190
	$1 - \{ 0 \}$	· · · · · · · · · · · · · · · · · · ·			IN 0-52 IN 53-78 IN 53-78 IN 59-91 IN 79-91 IN 92-104 IN 92-104 FA 28 FA 30 FA 30 FA 33 FA 33 FA 33 FA 33 FA 33 FA 35 FA 35 FA 50 FA 50 FA 50 FA 50 FA 50 FA 52 FA 52 FA 54	2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1				0.190

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Analysis of Carcinogenic Potential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 19, 1997 (8:40)

Source: c:\\_data\hemice.txt

Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL Note:

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some) Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively

ORGAN	ORGAN	TUMOR	TUMOR	TUMOR	TT LATE			VALUES	
NAME	CODE	NAME	CODE	TYPE	INTERVAL	ROW TABLE	EXACT PERMU	ASYMP- TOTIC	CONTINU CORRECT
					FA 57	2 .			
					FA 61	1			
					FA 61	2 1			
					FA 62	1			
					FA 62 FA 63	2 1 2 1			
					FA 63	2			
					FA 65	1			
					FA 65	2 1			
					FA 66	1			
					FA 66 FA 67	2 1			
					FA 67	, 2			
					FA 68	/ 1			
					FA 68 /	2			
					FA 69 /	1			
					FA 69 / FA 70	2 1	[15] T. S.		
					FA 70	2			
					FA 72	1			
					FA 72	2			
					FA 73 FA 73	1 2			
					FA 74	1			
					FA 74	2			
					FA 75	1			
					FA 75	2			
					FA 76 FA 76	1 2			
					FA 77	í			
					FA 77	2			
					FA 78	1. 1			
					FA 78	2			
					FA 79 FA 79	(1) (2)			
					A 80	1			
				- I	A 80	2			
					A 81	<b>1</b>			
					A 81	2			
					A 82 A 82	2			
				Ī	A 83	1			
				E	E9 A	2			
				F	A 84	1			
				F	A 84	2			
				F	A 85 A 85	1 2			
				È		í			
				F		2			
age -	2 - (Ove	r)							

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Analysis of Carcinogenic Fotential in Female Mouse Test of Dose-Response (Tumor) Positive Linear Trend Run Date & Time: March 19, 1997 (8:40)

Note:

Source: c:\\_data\hemice.txt
Dose Levels Included: CTR1 CTR2 LOW MED HIGH MAXI (0 0 25 375 750 1500)

For missing Tumor-Caused-Death set INCIDENTAL

IN: Incidental (nonfatal) to all, FA: Fatal to all, MX: Mixed (Fatal to some)

Symbols, ^ and + indicate that p-values are <0.005 and <0.025 respectively

ORGAN	ORGAN	TUMOR	TUMOR	My nam			P VALUES
NAME	CODE	NAME	CODE	TUMOR TYPE	INTERVAL	ROW TABLE	EXACT ASYMP- CONTINU PERMU TOTIC CORRECT
					FA 87	1	
					FA 87	2	
					FA 88	1	방문 등 하고 있는 글 사람들 만하는 것
					FA 88	2	항 별기 하장 등 등을 일으라고 있었다.
					FA 89		
					FA 89	1	
						2	문화 기존 등에 보고 있다. 그리고 하고 있다
					FA 90		를 모길 이 불리를 하는 것이 말 때문 모임이
					FA 90	2	얼마를 하고 하는 것이 글로벌 하다고 있다.
					FA 91	1	
					FA 91	2	
					FA 92	1	항상화가 하시다 이들이 나를 하였다.
					FA 92	2	
					FA 93	1	는 그들은 하다 가장 그를 가득하는 것은 사람들이 없었다.
					FA 93		
						/2	생각이 살아 보이 하는 것 같아 하는데 뭐 하는데 그 없다.
					FA 94	/ 1	
					FA 94 /	2	
					FA 95 /	1 1 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	
					FA 95	2	를 하고 있다면 살을 내는 것 같다 목욕을 다
		Tumor	ate: 90%	in CTL	- Total		그 항문을 하고 가고하다를 하고 있고 있는데 없다.
Page -	3 - (En	d of File)			Hereign H		얼마가 뭐 하지 않는 아무를 하면 하다 하는 것은

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## References

3

Lin et al (1994). "Statistical Review and Evaluation of Animal Tumorigenicity Studies." <u>Statistics in the Pharmaceutical Industry</u>. Marcel Dekker, Inc. pp. 19-57.

Thomas et al (1976). "Trend and Homogeneity Analyses of Proportions and Life Table Data." Computers and Biomedical Research. pp. 373-81.

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Haseman, J. K. (1983). "A re-examination of false-positive rates for carcinogenesis studies." | Fundamental and Applied Toxicology 3, pp. 334-9.

Haseman, J. K. (1984). "Issues in carcinogenicity testing: Dose selection." <u>Fundamental and Applied Toxicology</u>, Vol. 5. pp.

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